K110874

510(k) Summary

JAN 2 0 2012

Submitter information

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Date summary prepared: March 28, 2011

Device Trade or Proprietary Names:

ADVIA Chemistry β2-Microglobulin reagent
ADVIA Chemistry β2-Microglobulin calibrator

Device Common/Usual Name or Classification Name:

Beta-2-Microglobulin Immunological Test System
Calibrator

Classification Number / Class:

21 CFR 866.5630 – Beta-2-Microglobulin Immunological Test System Class II
21 CFR 862.1150 – Calibrator - Class II

Product code:

JZG – Beta-2-Microglobulin Immunological Test System
JIT – Calibrator, Secondary

This 510(k) summary of safety and effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92.

The assigned 510(k) number is: _____

Assay Predicate Device:

	Predicate Device
Device Name	Siemens N Latex β2 – Microglobulin (N B2M)
Common name	Beta-2-Microglobulin Immunological Test System – Class II
510(k) Number	k002731
Manufacturer	Siemens (formerly Dade Behring, Inc)

Calibrator Predicate Device

	Predicate Device
Device Name	Siemens N-protein standard SL
Common name	Calibrator, multi-analyte mixture
510(k) Number	k052788
Manufacturer	Siemens (formerly Dade Behring, Inc)

Device Description:

The ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay sample is diluted and reacted with a buffer that contains latex particles coated with antibody specific for β2-microglobulin. The formation of the antibody-antigen complex during the reaction results in an increase in turbidity, the extent of which is measured as the amount of light absorbed at 545 nm. The β2-Microglobulin concentration in a sample is determined by constructing a standard curve from the absorbance of a reagent blank and a single-level calibrator.

The ADVIA Chemistry β2-Microglobulin Calibrator is a single analyte, lyophilized, buffer based product containing bovine serum albumin and human β2-Microglobulin. The kit consists of 3 vials of a single level calibrator. The calibrator requires reconstitution with 1mL of distilled water prior to use.

Statements of Intended Use:

Reagent: for *in vitro* diagnostic use in the quantitative determination of β2-microglobulin in human serum or plasma (lithium heparin and potassium EDTA) on ADVIA® 1650 Chemistry systems. The ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay aids in the diagnosis of active rheumatoid arthritis and kidney disease.

Calibrators: for *in vitro* diagnostic use in the calibration of ADVIA® Chemistry systems for the ADVIA Chemistry β2-Microglobulin method.

Comparisons to the Predicate Devices:

Assay Similarities

Items	ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay	Siemens N Latex β2 - Microglobulin (N B2M) (Predicate Device) k002731
Similarity		
Intended Use/Indication for use	for *in vitro* diagnostic use in the quantitative determination of β2-microglobulin in human serum or plasma (lithium heparin and potassium EDTA) on ADVIA® 1650 Chemistry systems. The ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay aids in the diagnosis of active rheumatoid arthritis and kidney disease.	Similar The Siemens N Latex β2 - Microglobulin (N B2M) is *In vitro* diagnostic reagent for the quantitative determination of β2-microglobulin in human serum, plasma (EDTA and heparinized), as well as in urine by means of particle-enhanced immuno-nephelometry on the BN Systems. This assay aids in the diagnosis of renal dysfunction.
Measurement	Quantitative	Same
Reagent storage temperature	2-8°C	Same
Format	Liquid	Same
Use of Calibrators	Yes	Same
Reference Range	1.0 to 2.4 mg/L	Similar 1.09 to 2.53 mg/L

Assay Differences

Items	ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay	Siemens N Latex β2 - Microglobulin (N B2M) (Predicate Device) k002731
Differences		
Platform	ADVIA 1650 Chemistry System	BN system
Assay principle	turbidimetric	nephelometric
On Board stability	21 days	Minimum 5 days
Sample Type	Serum, plasma	Serum, plasma, urine
Assay Range	0.25 – 18.0 mg/L	0.7 – 23.0 mg/L (serum/plasma)
Antibody Source	goat	mouse

Calibrator Similarities

Items	ADVIA Chemistry β2-Microglobulin Calibrator	Siemens N Protein Standard SL (Predicate Device) k052788
Similarities		
Intended Use/Indication for use	for *in vitro* diagnostic use the calibration of ADVIA® Chemistry systems for the ADVIA Chemistry β2-Microglobulin method.	Similar For *in vitro* diagnostic use for establishment of reference curves for the determination of 27 analytes including β2-Microglobulin on the BN Systems.
Number of calibrators	1	Same
Calibrator storage temperature	2-8°C	Same
Fill volume	1.0mL	Same
Traceability	WHO 1st International Standard	Same

Calibrator Differences

Items	ADVIA Chemistry β2-Microglobulin Calibrator	Siemens N Protein Standard SL (Predicate Device) k052788
Differences		
Analyte	Single	Multi
Format	Lyophilized – buffer based	Liquid – serum based
Stability	30 days after reconstitution	14 days after opening
Instrument	ADVIA 1650 Chemistry System	BN Systems

Performance:

Substantial equivalence for the ADVIA 1650 Chemistry β2-Microglobulin assay to the predicate device was demonstrated by testing several method performance characteristics including analytical sensitivity, linearity, imprecision, method comparison and interfering substances. The following information summarize the analytical sensitivity, linearity, precision (total), interfering substances, serum / plasma equivalency and method comparison results.

All of the evaluation studies gave acceptable results compared to the predicate device. These studies support that the ADVIA 1650 Chemistry β2-Microglobulin assay is substantially equivalent to the Siemens N Latex β2 -Microglobulin (N B2M) that is currently marketed.

Analytical Sensitivity

The Limit of Detection (LoD) and Limit of Blank (LoB) were determined by following CLSI guideline EP-17A. The study was performed by running 60 replicates of a blank (serum sample with a low concentration of β2-Microglobulin at < 0.20 mg/L) and 60 replicates of a low serum sample (serum sample with approximate concentration of 0.74mg/L). The following results were obtained:

LoB = 0.20 mg/L
LoD = 0.25 mg/L

Imprecision

Imprecision was assessed by assaying 4 serum based samples 2 times per run, 2 runs per day, for at least 20 days. Precision estimates were calculated according to CLSI document EP5-A2. The following results were obtained.

Table 1 – summary of Precision for the ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay

ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay	
Level (mg/L)	Total CV (%) n = 80
0.74	3.3
1.77	2.6
3.68	2.4
12.52	2.1

Interfering Substances

Interfering substances were tested at β2-microglobulin concentrations of approximately 1, 3 and 11 mg/L on the ADVIA 1650 chemistry β2-microglobulin assay. Table 2 summarizes the data for bilirubin (conjugated and unconjugated), hemolysis, lipemia (from intralipid), rheumatoid factor and ascorbic acid. Table 3 summarizes the data for acetone, cholesterol, creatinine, ethanol, glucose, IgG, IgM, riboflavin, total protein, urea, and uric acid.

Table 2

Interferent	Interferent Level	β_2-Microglobulin Sample Concentration	Interference
Bilirubin	60 mg/dL	1.14 mg/L	NSI*
(conjugated and	(1026 µmol/L)	10.95 mg/L	NSI*
unconjugated)			
Hemolysis	1000 mg/dL	1.27 mg/L	NSI*
(hemoglobin)	(10.0 g/L)	11.00 mg/L	NSI*
Lipemia**	1000 mg/dL	1.20 mg/L	NSI*
(from Intralipid)	(11.3 mmol/L)	11.03 mg/L	NSI*
Rheumatoid Factor (RF)	2500 IU/mL	1.16 mg/L	NSI*
		10.30 mg/L	NSI*
Ascorbic Acid	50 mg/dL	1.21 mg/L	NSI*
	100 mg/dL	1.21 mg/L	-15.3%
	150 mg/dL	10.73 mg/L	NSI*
	200 mg/dL	10.73 mg/L	-13.4%

*NSI = No Significant Interference. A percentage effect ≥ 10% is considered a significant interference.

Table 3

Substance in Serum	Concentration Tested	Interference
Acetone	up to 250 mg/dL	NSI*
Cholesterol	up to 500 mg/dL	NSI*
Creatinine	up to 125 mg/dL	NSI*
Ethanol	up to 1000 mg/dL	NSI*
Glucose	up to 2000 mg/dL	NSI*
Immunoglobulin G	up to 5000 mg/dL	NSI*
Immunoglobulin M	up to 1600 mg/dL	NSI*
Riboflavin	up to 15 mg/dL	NSI*
Total protein	up to 12 g/dL	NSI*
Urea	up to 60 mg/dL	NSI*
Uric acid	up to 12 mg/dL	NSI*

*NSI = No Significant Interference. A percentage effect ≥ 10% is considered a significant interference.

Correlation

A total of 88 samples serum samples were analyzed on the ADVIA 1650 Chemistry system using β2-Microglobulin reagent and on the Siemens N Latex β2 -Microglobulin (predicate device), in parallel on the same day to demonstrate the equivalence of the two methods.

Table 4 summarizes the data.

Table 4 - ADVIA 1650 Chemistry β2-microglobulin assay vs. Siemens N Latex β2 - Microglobulin (N B2M) method

Siemens N Latex β2 -Microglobulin vs ADVIA 1650 Chemistry B2M Assay					
X Axis	**Y Axis**	**n**	**r**	**Slope**	**Y-int**
Siemens N Latex β2 - Microglobulin	**ADVIA 1650 Chemistry B2M**	**88**	**0.99**	**1.03**	**-0.38**

Serum / Plasma (lithium heparin and EDTA)

The ADVIA 1650 Chemistry Centaur β2-microglobulin assay was evaluated using different sample tube collection types. A matrix study was performed using matched specimens drawn in different tube types, potassium EDTA and lithium heparin. β2-microglobulin values ranged from 0.97 to 17.75 mg/L. Linear regression analysis was performed using the following:

- serum (x) vs. potassium EDTA (y1)
- serum (x) vs. lithium heparin (y2)

No significant differences between tube types was observed. The following results were obtained:

Table 5

Specimen Type	Comparison Assay (x)	N	Regression Equation	Sy.x	r	Sample Range
Plasma (K_2EDTA)	ADVIA 1650/1800 B2M Reagent	57	y = 1.00x - 0.04	0.19	0.99	0.97–17.75 mg/L
Plasma (Lithium Heparin)	ADVIA 1650/1800 B2M Reagent	57	y = 1.01x + 0.01	0.21	0.99	0.97–17.75 mg/L

Conclusions:

The Siemens Healthcare Diagnostics ADVIA 1650 Chemistry Centaur β2-microglobulin assay ADVIA is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Siemens N Latex β2 -Microglobulin (N B2M) k002731.

The Siemens Healthcare Diagnostics ADVIA Chemistry β2-Microglobulin calibrator is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Siemens N Protein Standard SL k052788.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Siemens Healthcare Diagnostics, Inc.
c/o Mr. Neil Parker
Sr. Regulatory Affairs Specialist
511 Benedict Ave
Tarrytown, NY 10591

JAN 2 0 2012

Re: k110874
ADVIA® Chemistry β2-Microglobulin Reagent
Regulation Number: 21 CFR §866.5630
Regulation Name: Beta-2-Microglobulin Immunological Test System
Regulatory Class: II
Product Code: JZG, JIT
Dated: January 10, 2012
Received: January 12, 2012

Dear Mr. Parker:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Reena Philip

for Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K110874
Device Name: ADVIA 1650 Chemistry β2-microglobulin (B2M) method
Indication for Use:

Reagent: for *in vitro* diagnostic use in the quantitative determination of β2-microglobulin in human serum or plasma (lithium heparin and potassium EDTA) on ADVIA 1650 Chemistry systems. The ADVIA 1650 Chemistry β2-Microglobulin (B2M) assay aids in the diagnosis of active rheumatoid arthritis and kidney disease.

Calibrator: for *in vitro* diagnostic use in the calibration of ADVIA® Chemistry systems for the ADVIA Chemistry ß2-Microglobulin method

Prescription Use X And/Or Over the Counter Use_____
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K110874